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10                   **AMPLIFIABLE ADENO-ASSOCIATED VIRUS (AAV)**  
**PACKAGING CASSETTES FOR THE PRODUCTION OF RECOMBINANT AAV**  
**VECTORS**

TECHNICAL FIELD

15           This invention is in the field of viral constructs for gene delivery. More specifically, the invention is in the field of recombinant DNA constructs for use in the production of adeno-associated virus (AAV) vectors for gene delivery.

BACKGROUND

20           Vectors based on adeno-associated virus (AAV) are believed to have utility for gene therapy but a significant obstacle has been the difficulty in generating such vectors in amounts that would be clinically useful for human gene therapy applications. This is a particular problem for *in vivo* applications such as direct delivery to the lung. Another important goal in the gene therapy context, discussed in more detail herein, is the production of vector preparations that are essentially free of replication-competent virions.

25           The following description briefly summarizes studies involving adeno-associated virus and AAV vectors, and then describes a number of novel improvements according to the present invention that are useful for efficiently generating high titer recombinant AAV vector (rAAV) preparations suitable for use in gene therapy.

30           Adeno-associated virus is a defective parvovirus that grows only in cells in which certain functions are provided by a co-infecting helper virus. General reviews of AAV may be found in, for example, Carter, 1989, Handbook of Parvoviruses, Vol. I, pp. 169-228, and Berns, 1990, Virology, pp. 1743-1764, Raven Press, (New York). Examples of co-infecting viruses that provide helper functions for AAV growth and replication are adenoviruses, herpesviruses and, in some cases, poxviruses such as vaccinia. The nature of



















































































































